

ABSTRACT OF THE DISCLOSURE

Covalently bound non-polar tags are used to increase the retention times of double stranded polynucleotides on Matched Ion Polynucleotide Chromatography (MIPC) columns. In doing so, separations of DNA mixture components is improved. Additionally, when the non-polar tags are fluorophores, detection limits are also greatly reduced. Strategically tagged primers are used in conduction with PCR to produce DNA fragments having specifically tagged strands. This improves mutation detection by MIPC in several ways. Separations are improved, detection sensitivity is enhanced, and non-stoichiometric addition of wild type DNA prior to hybridization is now possible since only tagged fragments will be observed with a fluorescence detector. Non-polar tags are also used as a novel alternative to G-C clamping during MIPC under partially denaturing conditions. Reversible DNA binding dyes, such as DNA intercalator dyes and DNA groove binding dyes, are used to reduce the detection limit of polynucleotides separated by MIPC.